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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/458,299	12/10/1999	JOHN FIKES	18623-014800	8698

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/458,299	FIKES ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41,45-48,50-54,58,64,65 and 93-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41,45-48,50-54,58,64,65 and 93-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *both filed 1/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. Applicant's amendment filed 12/22/04 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election without traverse of the species of peptide SEQ ID NO: 4233 KVFGSLAFV in Applicant's response filed 9/2/03 and species of 9 amino acid residues in length, a fusion heteropolymer comprising the said peptide and composition thereof in Applicant's response filed 2/23/04.

Claims 41, 45-48, 50-54, 58, 64, 65 and 93-97 are currently being examined.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The declaration is defective because: Inventors Celis, Chestnut and Fikes have not signed the declaration. In addition, the amendment referred to in the declaration should be listed as having been filed on 9/17/01 rather than 9/7/01.

The following are new grounds of rejection necessitated by Applicant's amendment filed 12/22/04.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 45-48, 51, 54, 58, 64, 65 and 93-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed peptide composition and linked polypeptide/ composition thereof comprising SEQ ID NO: 4233 and further comprising one or more different immunogenic peptides that are not Th epitope peptides or TAA (tumor associated antigen) peptides.

The instant claims encompass peptides/compositions thereof comprising SEQ ID NO: 4233 and *any* other immunogenic peptide(s) or any lipid. There is insufficient disclosure in the specification such compositions comprising other peptides that are not Th epitope peptides or TAA peptides (CTL epitopes) or peptides that induce antibody production to elicit immunity for the same tumor target.

The instant specification discloses Her-2/neu peptides linked to carriers or linked as homopolymers or heteropolymers, and where different peptide epitopes are used to make up the polymer, and the ability to induce antibodies and/or CTLs that react with different antigenic determinants of the tumor-related peptide targeted for an immune response (last paragraph on page 42). The specification further discloses that an epitope-based anti-tumor vaccine provides the opportunity to combine epitopes derived from multiple tumor-associated molecules (page 7 at lines 9-10).

There is no disclosure of compositions comprising other peptides that are not Th epitope peptides or TAA CTL epitope peptides. One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Applicant's arguments in Applicant's amendment have been fully considered, but are not persuasive.

Applicant's position is of record in the paragraph spanning pages 10 and 11 of the said amendment, briefly that the claims have been amended to recite "an immunogenic peptide" which is described in the application as "a peptide that comprises an allele-specific motif or supermotif such that the peptide will bind an HLA molecule and induce a CTL and/or HTL response".

It is the Examiner's position that the specification discloses peptide compositions comprising a tumor associated antigen such as SEQ ID NO: 4233 in a composition with or linked to another tumor associated antigen, not any immunogenic peptide from any source.

6. Claims 45-48, 51, 54, 58, 64, 65 and 93-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how make and or/use a peptide composition and a linked polypeptide/composition thereof comprising the peptide consisting of SEQ ID NO: 4233 and further comprising one or more different immunogenic peptides that are not Th epitope peptides or TAA (tumor associated antigen) peptides.

The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass compositions comprising SEQ ID NO: 4233 and *any* other immunogenic peptide(s).

The instant specification discloses her-2/neu peptides linked to carriers or linked as homopolymers or heteropolymers, and where different peptide epitopes are used to make up the polymer, the additional ability to induce antibodies and/or CTLs that react with different antigenic determinants of the tumor-related peptide targeted for an immune response (last paragraph on page 42). The specification further discloses that an epitope-based anti-tumor vaccine provides the opportunity to combine epitopes derived from multiple tumor-associated molecules (page 7 at lines 9-10).

Evidentiary reference WO 01/00225 A1 (Applicant's IDS reference) teaches that epitopes have been identified on target molecules such as Her2/neu (especially page 10 at the last paragraph). WO 01/00225 A1 further teaches that CTL epitope peptides may be combined with HTL (Th) epitope peptides in order to increase immune reactivity (especially page 24 at the first two paragraphs). WO 01/00225 A1 teaches that polymers of the different peptide epitopes have the additional ability to induce antibodies and/or CTLs that react with different antigenic determinants of the tumor-related peptide (i.e., protein) targeted for an immune response (especially page 27 at the first full paragraph).

There is insufficient disclosure in the specification such compositions comprising other peptides that are not Th epitope peptides or TAA peptides (CTL epitopes) or peptides that induce antibody production to elicit immunity for the same tumor target. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in Applicant's amendment have been fully considered, but are not persuasive.

Applicant's position (of record on pages 12-16 of the said amendment) does not speak to the issues in the instant rejection, and is therefore moot.

It is the Examiner's position that the specification discloses peptide compositions comprising a tumor associated antigen such as SEQ ID NO: 4233 in a composition with or linked to another tumor associated antigen, not any immunogenic peptide from any source.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 45-48, 51, 64, 65 and 93-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicant regards as the invention.

Claims 45-48, 51, 93 and 94 are indefinite in the recitation of "linked polypeptide" because it is not clear what is meant. It appears that the components of the polypeptide are linked, but the polypeptide is not.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 41, 52, 54 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (Human Immunology 59, 1-14, 1/1998, Applicant's IDS reference) in view of Sidney et al (Immunology Today 17(6), 261-266, 1996, of record) and Rowland-Jones (J. Clin. Invest. 102(9), 1758-1765, 11/1998, of record).

Kawashima et al teach identification of nonamer and decamer peptides containing HLA-A2.1 binding motifs from Her-2/neu tumor associated antigen protein, that out of 165 peptides possessing the motifs, 23 were found to bind to HLA-A2.1 with an $IC_{50}\leq$ 500 nm (about 8%), and that the majority of CTL epitopes bind to their respective class I molecules with $IC_{50}\leq$ 500 nm, i.e., with intermediate to high affinity (especially page 7, column 1 at lines 2-9 and the paragraph spanning columns 1 and 2 on page 9). Kawashima et al teach that one of the identified peptides, the Her2[369] peptide KIFGSLAFL, binds to HLA-A2.1 with high affinity and is a CTL epitope in cancer patients (especially page 7, column 1 at lines 2-9). Kawashima et al teach binding of the 369 peptide to supertype motif alleles (especially Table 4 and Table 3 and page 6 at the last paragraph and continuing onto page 7 through the paragraph spanning columns 1 and 2). Kawashima et al further teach that the said peptide epitope binds with high affinity to four HLA-A2 supertype alleles, but binds with very low affinity to a fifth HLA-A2 supertype allele, HLA-A*6802, i.e., with an IC_{50} of 3,333 (especially Table 4). Kawashima et al teach that HLA-A68.2 was chosen because of the high frequency of HLA-A*6802 in the black population (especially paragraph spanning pages 7 and 8).

Kawashima et al teach cocktails of the peptide with other peptides and pharmaceutical carriers (especially last paragraph). Kawashima et al teach that an immunotherapeutic approach should satisfy the condition of broad and non-ethically biased coverage of patient populations (especially page 10, column 1 at the first full paragraph).

Kawashima et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application) nor the said peptide in a composition comprising a carrier, including a pharmaceutically acceptable carrier, or one or more different immunogenic peptides.

Sidney et al teach the A2-like binding supertype alleles include the HLA alleles listed in Table 4 of Kawashima et al, and in addition include HLA-A*6901 among others listed in Table 3 of Sidney et al. Sidney et al further teach the supermotif for binding to the HLA-A2-like alleles is A/I/L/M/V/T at position two of the peptide for binding of the side chain of the P2 amino acid residue in the B pocket of HLA and A/I/L/M/V/T at the carboxy-terminus of the peptide for binding of the side chain of the carboxy-terminal amino acid residue in the F pocket of HLA (especially Table 4). Sidney et al teach the advantage of using epitopes that bind to supertype alleles for greater coverage in populations (especially page 261 at the paragraph spanning columns 1 and 2).

Rowland-Jones et al teach use of a V/T at P2 and V/L at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the CTL epitope Her2[369] peptide KIFGSLAFL taught by Kawashima et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Sidney et al or for peptides that bind to HLA-A2-like supertype alleles as taught by Sidney et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to satisfy the condition taught by Kawashima et al of broad and non-ethically biased coverage of patient populations, i.e., to make a peptide that would bind with intermediate to high affinity to all HLA-A2 supertype alleles, by making a peptide that would bind with higher affinity to the HLA-A*6802 allele because Kawashima et al teach that the parent peptide epitope KIFGSLAFL binds to HLA-A*6802 with low affinity and that the HLA-A*6802 allele is present in high frequency in the black population, and Sidney et al teach the supermotif for binding to HLA-A2-like alleles (which includes HLA-A*6802) includes a V at position 2 and position 9 and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802.

Applicant's arguments in Applicant's amendment filed 12/22/04 have been fully considered but are not persuasive.

Applicant's arguments are of record in the said amendment on pages 18-24, briefly that: (1) one of skill in the art would not have been motivated to choose the single epitope KIFGSLAFL from the 23 Her2/neu peptides discussed in Kawashima et al and would not have been motivated by Sidney or Rowland Jones to modify the said peptide to arrive at the claimed peptide; (2) there is no motivation to combine Rowland Jones with Kawashima et al because Rowland Jones is directed to HIV not cancer; (3) the combination of Kawashima and Sidney suggest a possible 64 peptides that would potentially bind to HLA-A2-like alleles, and that the claimed peptide is only one member of a genus of predicted peptides; (4) Rowland Jones teaches that they used information about the B and F pockets to predict a motif for HLA-A68.2, which is an insufficient basis for one of skill in the art to have concluded that V/T at position 2 and V/L at position 9 was a binding motif for HLA-A68.2; (5) Rowland Jones teaches that out of 49 predicted peptides from Her2/neu, only four were recognized by CTL (about 8%) and only two contained V at both anchor positions, and there was no indication that the V2V9 combination was better than the peptides with other subcombinations of the VTP2/VLP9 motif.

It is the Examiner's position that: (1) Kawashima et al provide motivation to have chosen the KIFGSLAFL peptide because they teach that it is a CTL epitope in cancer patients that binds to HLA-A2.1 with high affinity, as well as to three other HLA-A2 supertype alleles with high affinity, and to the fourth other allele HLA-A68.2 with very low affinity, and that peptides that serve as immunogenic peptides generally bind to their respective HLA class I molecules with intermediate to high affinity; (2) Rowland Jones is relied upon for the teaching of a motif for peptides that bind to HLA-A68.2, and one of ordinary skill in the art at the time the invention was made was aware that peptides from Her2/neu also possess binding motifs for binding to class I molecules since Kawashima et al teach peptides that bind to class I HLA-A2 supertype alleles from Her2/neu and treatment of cancer with the peptides, as does Rowland Jones for the HIV peptides and treatment of HIV infection; (3) Kawashima et al teach that the KIFGSLAFL peptide is a CTL epitope that binds to HLA-A2.1 and three other HLA-A2 supertype alleles with high affinity, Sidney teaches a motif for peptides that bind to HLA-A2 supertype alleles, Rowland Jones teaches a motif for peptides that bind to HLA-A68.2 that consists of two potential anchor residue amino acids at each of the two dominant anchor residues, i.e., one peptide KIFGSLAFL, modified with 4 different potential combination of anchor residues; (4) Rowland Jones teaches a motif predicted using knowledge of the HLA-A68.2 pocket amino acid residues that bind the side chains of the amino acid residues at dominant anchor positions of peptides and then subsequently confirmed recognition by CTL assay (and thus also indirectly confirmed binding also for these four recognized peptides) and such teaching provides one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. One of skill in the art at the time the invention was made was aware that motif analysis was accomplished in a variety of ways, including isolation of endogenous peptides, epitope mapping using overlapping peptide subsequences of immunogenic proteins, epitope mapping using successively smaller portions of immunogenic proteins, prediction based upon

knowledge of the HLA pocket amino acid residues, amino acid residue substitution analysis of individual peptides, etc; (5) Rowland Jones teaches that 8% of the predicted peptides were recognized by CTL, but does not address how many bound but were not recognized, and so the 8% was comparable and possibly higher to that taught by Kawashima et al using their HLA binding motif. In addition, Rowland Jones provides a motif that is within the motif taught by Sydney for HLA-A2 supertype alleles and further narrows it for HLA-A68.2. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made all four combinations of the substituted peptide, since the parent peptide was already known to be immunogenic and the residues that were being substituted were selected to boost affinity of binding to HLA-A68.2 without changing the TCR recognition residues. One of ordinary skill in the art would have been motivated to do this in order to produce a peptide that would bind to HLA-A68.2 with higher affinity than the parent peptide to be used for immunizing an HLA-A68.2 positive or containing patient population.

11. Claims 45-48, 50, 51, 53, 64, 65 and 93-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (Human Immunology 59, 1-14, 1/1998, Applicant's IDS reference) in view of Sidney et al (Immunology Today 17(6), 261-266, 1996, of record) and Rowland-Jones (J. Clin. Invest. 102(9), 1758-1765, 11/1998, of record) as applied to claims 41, 52, 54 and 58 above and further in view of WO 95/19783A1 (of record).

Kawashima et al teach identification of nonamer and decamer peptides containing HLA-A2.1 binding motifs from Her-2/neu tumor associated antigen protein, that out of 165 peptides possessing the motifs, 23 were found to bind to HLA-A2.1 with an $IC_{50} \leq$ 500 nm (about 8%), and that the majority of CTL epitopes bind to their respective class I molecules with $IC_{50} \leq$ 500 nm, i.e., with intermediate to high affinity (especially page 7, column 1 at lines 2-9 and the paragraph spanning columns 1 and 2 on page 9). Kawashima et al teach that one of the identified peptides, the Her2[369] peptide KIFGSLAFL, binds to HLA-A2.1 with high affinity and is a CTL epitope in cancer patients (especially page 7, column 1 at lines 2-9). Kawashima et al teach binding of the 369 peptide to supertype motif alleles (especially Table 4 and Table 3 and page 6 at the last paragraph and continuing onto page 7 through the paragraph spanning columns 1 and 2). Kawashima et al further teach that the said peptide epitope binds with high affinity to four HLA-A2 supertype alleles, but binds with very low affinity to HLA-A*6802, i.e., with an IC_{50} of 3,333 (especially Table 4). Kawashima et al teach that HLA-A68.2 was chosen because of the high frequency of HLA-A*6802 in the black population (especially paragraph spanning pages 7 and 8). Kawashima et al teach cocktails of the peptide with other peptides and pharmaceutical carriers (especially last paragraph). Kawashima et al teach that immunotherapeutic approach should satisfy the condition of broad and non-ethically biased coverage of patient populations (especially page 10, column 1 at the first full paragraph).

Kawashima et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application), nor the said peptide in a composition comprising a carrier, including a pharmaceutically acceptable carrier, a liposome or one or more different immunogenic peptides, nor the said peptide/composition thereof linked to one or more of a Th peptide including the universal Th epitiope SEQ ID NO: 4266 (akXVWANTLKAAa) recited in instant claim 65, spacer molecule(s), a carrier, a lipid, or one or more different immunogenic peptides, including wherein said composition further comprises a carrier or a liposome, nor the peptide linked to itself as a homopolymer.

Sidney et al teach the A2-like binding supertype alleles include the HLA alleles listed in Table 4 of Kawashima et al, and in addition include HLA-A*6901 among others listed in Table 3 of Sidney et al. Sidney et al further teach the supermotif for binding to the HLA-A2-like alleles is AILMVT at position two of the peptide for binding of the side chain of the P2 amino acid residue in the B pocket of HLA and AILMVT at the carboxy-terminus of the peptide for binding of the side chain of the carboxy-terminal amino acid residue in the F pocket of HLA (especially Table 4). Sidney et al teach the advantage of using epitopes that bind to supertype alleles for greater coverage in populations (especially page 261 at the paragraph spanning columns 1 and 2).

Rowland-Jones et al teach use of a VT at P2 and VL at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph).

WO 95/19783A1 teaches the universal Th (T helper) peptide aKSVWANTLKAAa (SEQ ID NO: 4226 of the instant claim 65) (especially claim 21 and the paragraph spanning pages 14 and 15) linked to an immunogenic peptide. WO 95/19783A1 further teaches an immunogenic peptide/pharmaceutical compositions thereof linked to a lipidated peptide, or to Th epitopes or to carriers in order to increase immunogenicity of a peptide, and wherein spacer or linker amino acid residues are added (especially claims 18 and 19, page 13 at paragraph 1 and 2, page 14, and page 8 at paragraph 3). WO 95/19783A1 teaches that the peptides are between about 8 and about 20 residues, preferably 9 or 10. WO 95/19783A1 teaches substituted peptides for change in function such as affinity of binding to MHC or to TCR (especially page 12). WO 95/19783A1 also teaches fusion proteins comprising one or more immunogenic peptides (especially pages 16 at the third paragraph) and pharmaceutical compositions thereof (especially page 19) and administration via liposomes (especially pages 19 and 20).
WO 95/19783A1 teaches homo or heteropolymers of the said immunogenic peptides/compositions thereof (especially page 21 at paragraph 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the CTL epitope Her2[9369] peptide KIFGSLAFL taught by Kawashima et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that

bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Sidney et al or for peptides that bind to HLA-A2-like supertype alleles as taught by Sidney et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have fused the peptide(s) to a Th peptide such as the universal Th peptide epitope taught by WO 95/19783A1 as taught by WO 95/19783A1 for other immunogenic CTL epitope peptides, to have fused the peptide(s) to linker amino acid residues and to a carrier or link it to a lipid or to administer it via a liposome, or to make it as a homo or heteropolymer or a composition comprising more than one immunogenic peptide as taught by WO 95/19783A1 for other immunogenic peptides, and including use of spacer molecules between peptides.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to satisfy the condition taught by Kawashima et al of broad and non-ethically biased coverage of patient populations, i.e., to make a peptide that would bind with intermediate to high affinity to all HLA-A2 supertype alleles, by making a peptide that would bind with higher affinity to the HLA-A*6802 allele because Kawashima et al teach that the parent peptide epitope KIFGSLAFL binds to HLA-A*6802 with low affinity and that the HLA-A*6802 allele is present in high frequency in the black population, and Sidney et al teach the supermotif for binding to HLA-A2-like alleles (which includes HLA-A*6802) includes a V at position 2 and position 9 and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a more effective peptide composition capable of stimulating an immune response, as taught for the fusion peptides, or lipid linked peptides or liposome administered peptides taught by WO 95/19783A1.

Applicant's arguments in Applicant's amendment filed 12/22/04 have been fully considered but are not persuasive.

Applicant's arguments are of record in the said amendment on pages 25-26, and are addressed to the same issues as the rejection set forth at item #10 supra.

The Examiner's arguments set forth at item #11 supra apply herein.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 41, 45-48, 50-54, 58, 64, 65 and 93-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 and 15-27 of copending Application No. 10/149,138 (US2004/0121946A9, corrected publication of US2004/0018971 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other SEQ ID NO: 4233 of the instant application is in Table XXVII of the 10/149,138, and the SEQ ID NO: 4226 universal T helper epitope of instant claim 65 is an obvious variant as evidenced by the disclosure of the HTL epitope in 10/149,138 to be a pan-DR universal Th epitope (on page 20 at paragraph 0219). Instant claim 46 is included in this rejection because it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included spacer molecules between peptides in order to facilitate processing and avoid creation of neoepitopes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 41, 45-48, 50-54, 58, 64, 65 and 93-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-13, 18-31 and 35-37 of copending Application No. 10/149,915 (US2003/0224036 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because copending Application No. 10/149,915 recites in claim 1 and claim 18 SEQ ID NO: 4233 of the instant claims, and the SEQ ID NO: 4226 universal T helper epitope of instant claim 65 is an obvious variant of the genus as evidenced by the disclosure of the HTL epitope in Application No. 10/149,915 on page 18 at paragraph 0180.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. The reference AL3 crossed out in the Forms 1449 filed 1/11/05 has not been considered because a translation has not been provided by Applicant.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino

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March 28, 2005

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